Claims

1. A crystalline polymorph B of 3-[[(1S)-1-(ethoxy-carbonyl)-3-phenylpropyl]amino]-2,3,4,5-tetrahydro-2-oxo-1H-1-benzazepine-1-acetic acid monohydrochloride which exhibits a characteristic X-ray powder diffraction pattern with characteristic peaks expressed in d-values (Å) at 13.2 (vs), 10.7 (s), 8.8 (m), 6.4 (m), 5.87 (s), 5.75 (m), 5.35 (m), 5.26 (m), 4.87 (m), 4.66 (s), 4.40 (m), 3.86 (m), 3.79 (m), 3.66 (m), 3.60 (m), 3.57 (m), 3.52 (m), 3.45 (m), 3.40 (m), 3.36 (m), 3.27 (m), 3.18 (m), 2.95 (m), 2.72 (m), 2.65 (m); wherein (vs) = very strong intensity; (s) = strong intensity; (m) = medium intensity.

2. A crystalline polymorph B of 3-[[(1S)-1-(ethoxy-carbonyl)-3-phenylpropyl]amino]-2,3,4,5-tetrahydro-2-oxo-1H-1-benzazepine-1-acetic acid monohydrochloride having an X-ray powder diffraction pattern substantially as depicted in figure 2.

3. A crystalline polymorph B of 3-[[(1S)-1-(ethoxy-carbonyl)-3-phenylpropyl]amino]-2,3,4,5-tetrahydro-2-oxo-1H-1-benzazepine-1-acetic acid monohydrochloride having an X-ray powder diffraction pattern substantially as depicted in figure 3.

4. An amorphous form of 3-[[(1S)-1-(ethoxy-carbonyl)-3-phenylpropyl]amino]-2,3,4,5-tetrahydro-2-oxo-1H-1-benzazepine-1-acetic acid monohydrochloride.

5. An amorphous form of 3-[[(1S)-1-(ethoxy-carbonyl)-3-phenylpropyl]amino]-2,3,4,5-tetrahydro-2-oxo-1H-1-benzazepine-1-acetic acid monohydrochloride having a powder X-ray diffraction pattern substantially as depicted in Figure 4.

6. A process for the preparation of a crystalline polymorph according to claim 1, wherein an aqueous solution of hydrochloride is added to a solution of the free base 3-[[(1S)-1-(ethoxy-carbonyl)-3-phenylpropyl]amino]-2,3,4,5-tetrahydro-2-oxo-1H-1-benzazepine-1-acetic acid monohydrochloride in an organic solvent.

7. A process according to claim 6, wherein the organic solvent is a C_3-C_{10}ketone, C_3-C_{10}acetate, C_2-C_{10}nitrile, C_1-C_{10}alcohol or C_2-C_{10}ether, or mixtures thereof.

8. A process for the preparation of a crystalline polymorph according to claim 1, wherein a suspension of Form A or the amorphous form 3-[[(1S)-1-(ethoxy-carbonyl)-3-phenyl-propyl]amino]-2,3,4,5-tetrahydro-2-oxo-1H-1-benzazepine-1-acetic acid monohydro-chloride is stirred in an organic solvent.

9. A process according to claim 8, wherein the organic solvent is a C_3-C_{10}ketone, C_3-C_{10}acetate, C_2-C_{10}nitrile, C_1-C_{10}alcohol or C_2-C_{10}ether, or mixtures thereof.

10. A process according to claim 8 or 9, wherein the organic solvent is selected from acetone, 1-butanol, 2-butanol, butyl actetate, tert- butylmethyl ether, cumene, dimetylsulfoxide, ethanol, ethylether, ethylformiate, heptane isobutylacetate, isopropyl acetate, methylacetate 3-methyl-1-butanol, methylethyl ketone.

11. A process according to claim 8 or 9, wherein the organic solvent is selected from acetone, methyl ethyl ketone; ethylacetate, isopropylacetate, acetonitrile, isopropylalcohol, methyl-tert.butyl ether and THF.

12. A process according to any of claims 8 to 11, wherein the organic solvent contains small amounts of water.

13. A process according to claim 12, wherein the amount of water is 0.1 to 15% by volume of the suspension of 3-[[(1S)-1-(ethoxy-carbonyl)-3-phenylpropyl]amino]-2,3,4,5-tetrahydro-2-oxo-1H-1-benzazepine-1-acetic acid monohydrochloride.

14. A process according to claim 13, wherein the amount of water is 0.5 to 10% by volume of the suspension of 3-[[(1S)-1-(ethoxy-carbonyl)-3-phenylpropyl]amino]-2,3,4,5-tetrahydro-2-oxo-1H-1-benzazepine-1-acetic acid monohydrochloride.

15. A process for the preparation of a crystalline polymorph according to claim 1 wherein a suspension of Form A or the amorphous form of 3-[[(1S)-1-(ethoxy-carbonyl)-3-phenylpropyl]amino]-2,3,4,5-tetrahydro-2-oxo-1H-1-benzazepine-1-acetic acid monohydrochloride is stirred in water.

16. A process according to any of claims 6 to 15, wherein 3-[[(1S)-1-(ethoxy-carbonyl)-3-phenylpropyl]amino]-2,3,4,5-tetrahydro-2-oxo-1H-1-benzazepine-1-acetic acid monohydrochloride is isolated by filtration and dried in air or vacuum.

17. A process according to any of claims 6 to 16, wherein seeding is carried out with crystals of the crystalline polymorph according to claim 1.

18. A process for the preparation of the amorphous form according claim 4 or 5, wherein a solution 3-[[(1S)-1-(ethoxy-carbonyl)-3-phenylpropyl]amino]-2,3,4,5-tetrahydro-2-oxo-1H-1-benzazepine-1-acetic acid monohydrochloride in an organic solvent or in water is evaporated to dryness.

19. A process according to claim 18, wherein the organic solvent is a C_3-C_{10}ketone.

20. A process according to claim 18 or 19, wherein the organic solvent is acetone.

21. A process for the preparation of crystalline polymorph Form A of 3-[[(1S)-1-(ethoxy-carbonyl)-3-phenylpropyl]amino]-2,3,4,5-tetrahydro-2-oxo-1H-1-benzazepine-1-acetic acid monohydrochloride, wherein a concentrated solution of 3-[[(1S)-1-(ethoxy-carbonyl)-3-phenylpropyl]amino]-2,3,4,5-tetrahydro-2-oxo-1H-1-benzazepine-1-acetic acid monohydrochloride in an organic solvent is mixed with a non-solvent.

22. A process according to claim 21, wherein the organic solvent is an C_1-C_{10}alcohol, tetrahydrofuran, N-methylpyrrolidone or N,N-dimethylformamide and the non-solvent is a C_4-C_{12}alkane or C_1-C_{10}acetate.

23. A process according to claim 21 or 22, wherein a solution of 3-[[(1S)-1-(ethoxy-carbonyl)-3-phenylpropyl]amino]-2,3,4,5-tetrahydro-2-oxo-1H-1-benzazepine-1-acetic acid monohydrochloride in a C_1-C_4alcohol is mixed with heptane.

24. A process according to any of claims 21 to 23, wherein seeding with crystals of the Form A of 3-[[(1S)-1-(ethoxy-carbonyl)-3-phenylpropyl]amino]-2,3,4,5-tetrahydro-2-oxo-1H-1-benzazepine-1-acetic acid monohydrochloride is carried out.

25. A pharmaceutical composition comprising an effective amount of a crystalline polymorphic form according to one of claims 1 to 3 or the amorphous form according to claims 4 or 5, and a pharmaceutically acceptable carrier.